RE: Propoxur Conference Call - 28 Feb 2011
Maija Mizens
to:
Kaitlin Keller
02/28/2011 05:08 PM
Cc:
"bruce.martin.b@bayer.com", Deborah Chadbourne, Jason Johnston, James McFadden, James Messina, Jonathan Toot, 'Kelly Hoskins', "larry.sheets@bayercropscience.com", Larry Nouvel, 'Melissa Beck', Michael Goodis, Steve Spaulding, Terri Considine, Tracy Perry, Zaida Figueroa
Hide Details
From: Maija Mizens <MMizens@central.com> Sort List...

To: Kaitlin Keller/DC/USEPA/US@EPA

Cc: "bruce.martin.b@bayer.com" <bruce.martin.b@bayer.com>, Deborah Chadbourne <debchad@rcn.com>, Jason Johnston <jjohnston@exponent.com>, James McFadden <jmcfadden@central.com>, James Messina <jmessina@exponent.com>, Jonathan Toot <JToot@wilresearch.com>, 'Kelly Hoskins' <KHoskins@SERGEANTS.com>, "larry.sheets@bayercropscience.com" <larry.sheets@bayercropscience.com>, Larry Nouvel <LNouvel@SERGEANTS.com>, 'Melissa Beck' <MBeck@wilresearch.com>, Michael Goodis/DC/USEPA/US@EPA, Steve Spaulding <SSpaulding@central.com>, Terri Considine <TConsidine@central.com>, Tracy Perry/DC/USEPA/US@EPA, Zaida Figueroa/DC/USEPA/US@EPA

History: This message has been replied to.

1 Attachment

image001.gif

Dear Kaitlin:

In answer to the questions posed by Ginger Moser and Elissa Reaves:

Dose selection for adult rats is based on AChE results from Bayer's acute neurotoxicity study. In that study, RBC and brain AChE activity was measured in satellite animals that received the same dose levels as the main study groups, with samples collected 45 min after

treatment (the time of peak clinical signs, when animals in the main study groups underwent neurobehavioral testing). Below is a table below summarizing the Bayer data, along with data from the Moser paper (our best estimate from the figures in the paper). We think these doses are well suited to produce an effect of sufficient magnitude to determine the time of peak effect at both ages and to help guide dose selection for the main studies. However, we will re-evaluate the situation as data become available.

		0.75 hr	
		Brain	**RBC**
0.3	PD17	5%	15%
1	PD17	15%	25%
2	adult	18%	19%
3	PD17	35%	50%
10	adult	47%	72%
10	PD17	62%	70%
25	adult	61%	83%

I hope we can get a call together on Wednesday. Larry Sheets and I are available Wednesday at 3:00PM CST. I am waiting to hear from the scientists at WIL, their participate is key to this project.

Thank you and regards,
Maija

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-----Original Message-----
From: Keller.Kaitlin@epamail.epa.gov [mailto:Keller.Kaitlin@epamail.epa.gov]
Sent: Monday, February 28, 2011 3:22 PM
To: Maija Mizens
Cc: bruce.martin.b@bayer.com; Deborah Chadbourne; Jason Johnston; James McFadden; James Messina; Jonathan Toot; 'Kelly Hoskins'; larry.sheets@bayercropscience.com; Larry Nouvel; 'Melissa Beck'; Goodis.Michael@epamail.epa.gov; Steve Spaulding; Terri Considine; Perry.Tracy@epamail.epa.gov; Figueroa.Zaida@epamail.epa.gov
Subject: Re: Propoxur Conference Call - 28 Feb 2011

Hello Maija,

Ginger Moser of the EPA Office of Research and Development, and Elissa Reaves of the OPP Human Effects Division reviewed the proposed doses for the propoxur time-course study and compared them to PND17 data. They have a couple of questions below; it would be helpful if you could answer them prior to our call.

1) Is the 50% inhibition based on RBC or brain?
2) What data are you basing the adult doses on? (The dose for adults may be too low.)

As for a reschedule, it seems that Wednesday would be the best day for us to try this week. Would 10:00 am or 3:00 pm EST work for you?

Thank you,

Kaitlin

Kaitlin Keller
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Risk Management & Implementation Branch III
Pesticide Re-evaluation Division, USEPA Office of Pesticide Programs
Phone: (703) 308-8172

From: Maija Mizens <MMizens@central.com>
To: Kaitlin Keller/DC/USEPA/US@EPA, Michael Goodis/DC/USEPA/US@EPA, Tracy Perry/DC/USEPA/US@EPA, Zaida Figueroa/DC/USEPA/US@EPA
Cc: "bruce.martin.b@bayer.com" <bruce.martin.b@bayer.com>, "larry.sheets@bayercropscience.com" <larry.sheets@bayercropscience.com>, 'Kelly Hoskins' <KHoskins@SERGEANTS.com>, Deborah Chadbourne <debchad@rcn.com>, Jason Johnston <jjohnston@exponent.com>, James Messina <jmessina@exponent.com>, Larry Nouvel <LNouvel@SERGEANTS.com>, James McFadden <jmcfadden@central.com>, Steve Spaulding <SSpaulding@central.com>, Terri Considine <TConsidine@central.com>, Jonathan Toot <JToot@wilresearch.com>, 'Melissa Beck' <MBeck@wilresearch.com>
Date: 02/25/2011 02:29 PM
Subject: Propoxur Conference Call - 28 Feb 2011

Dear Kaitlin:

In preparation for our conference call on Monday, I wanted to share some details about our proposal for the first phase of the CCA project. As I indicated in my earlier e-mail, the proposal is to start with the time course study.

The following is proposed for the study:

Doses are proposed at 3 mg/kg for the PND 11 and 5 mg/kg for adults. Data from Moser et al. and Bayer indicate that these doses will result in cholinesterase inhibition in the 50% range, which should be a good range for determining the peak cholinesterase activity.

Assay times are proposed at 0.25, 0.5, 1.0 and 2.0 hours. These times should adequately evaluate the time of peak activity. If the objective of this study extends to recovery, then an additional time point may be required. Propose to use only one sex (n=7), since data from Bayer indicate that there are no real differences between adult males and female for cholinesterase inhibition.

Since there are no data on the toxicity of propoxur to PND 11, some preliminary testing is proposed with the PND 11 pups to insure that the dose of 3 mg/kg is not too toxic to use for the time course study.

Doses for the dose range-finding study will be selected after the completion of the time course study. We would like to review the dose selection with the Agency before proceeding with the dose range-finding study.

Study schedule: The time course study can be initiated in late March or

early April. WIL is reviewing availability of space and resources and will propose a more detailed schedule after the conference call.

I hope this is useful in preparing for the call on Monday.

Thank you Kaitlin for all your efforts in organizing the call.

Maija

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